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RESEARCH ARTICLE

Synergistic Effect of Antibiotic Fucidic acid with *Cinnamomum zeylanicum* and *Curcuma longa* Extracts against *Escherichia coli and Staphylococcus aureus*

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ABSTRACT

The present study focused on evaluation of antibacterial effect of *Cinnamomum zeylanicum* and *Curcuma longa* extracts and their synergistic effect with some antibiotic. Antimicrobial activity of plant extracts against *Escherichia coli*. *C. longa* was showed the highest effect against *E. coli* with a zone of inhibition 13 and 14.5 mm at a concentration of 100 and 200 mg/mL, respectively. While antimicrobial activity was observed by *C. zeylanicum*, with a zone of inhibition 9 and 13.9 mm at a concentration of 100 and 200 mg/mL, respectively. Antimicrobial activity against *Staphylococcus aureus* with a zone of inhibition 11 and 16.8 mm at a concentration of 100 and 200 mg/mL, respectively, of *C. longa*. No antimicrobial activity was observed by *C. zeylanicum*, at a concentration of 100 mg/mL and a zone of inhibition 10 mm at a concentration of 200 mg/mL, antibiotics activity of Fucidic acid (50 mg, 100 mg) against *S. aureus* and *E. coli*. Fucidic acid was showed effectiveness against *S. aureus* and *E. coli* with a zone of inhibition 15 and 17 mm at a concentration of 50 mg, respectively. While was zone of inhibition 17.4 and 19 mm at a concentration of 100 mg against *S. aureus* and *E. coli,* respectively. Extract of *C. zeylanicum* increased the effectiveness of Fucidic acid against *E. coli* (17 mm). As for the *C. longa* extract was the results with Fucidic acid on the bacteria (22 mm). *C. zeylanicum* and *C. longa* extracts and antibiotics, extract of *Cinnamomum Zeylanicum* increased the effectiveness each of Fucidic acid against *S. aureus* (18.6 mm). As for the *C. longa* extract was the results (when added to antibiotics) almost similar to *C. zeylanicum* extract, where it also has increased the impact of Fucidic acid on the bacteria *S. aureus* (20.4 mm).

Keywords: *Cinnamomum zeylanicum, Curcuma longa*, Fucidic acid, synergistic

INTRODUCTION

Antibiotics can be described as a compound that works to either stop bacteria from growing (bacteriostatic agents) or by killing them entirely (bactericidal agents) (Sommer and Dantas, 2011). The WHO has listed seven bacteria of international concern; *Klebsiella pneumoniae, Escherichia coli, Staphylococcus aureus,* non-typhoidal *Salmonella* (NTS), *Neisseria gonorrhoeae, Shigella* species, *and Streptococcus pneumoniae* (Chaudhary, 2016).

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Medicinal plants are abundant in phytochemicals such as flavonoids, terpenoids, glycosides, and alkaloids, which have remedial antimicrobial potential (Ahmad *et al.,* 2015). Several studies have reported the broad-spectrum antimicrobial activity for curcumin including antibacterial, antiviral, antifungal, and antimalarial activities. Because of the extended antimicrobial activity of curcumin and safety property even at high doses (17 g/day) assessed by clinical trials in human, it was used as a structural sample to design the new antimicrobial agents with modified and increased antimicrobial activities through the synthesis of various derivatives related to curcumin (Anand *et al*., 2007).

Curcumin finished wool had semidurable antimi crobial activity, less durable to light exposure than

home laundering with 45% and 30% inhibition rates against *S. aureus* and *E. coli*, respectively, after 30 cycles of home laundering (Han and Yang, 2005). The antibacterial study on aqueous extract of *Curcuma longa* rhizome demonstrated the MIC value of 4–16 g/L and MBC value of 16–32g/L against *S. epidermis*, *S. aureus*, *K. pneumoniae*, and *E. coli* (Niamsa and Sittiwet, 2009). The methanol extract of turmeric revealed MIC values of 16 μg/mL and 128 μg/mL against *Bacillus subtilis* and *Staph. aureus*, respectively (Ungphaiboon *et al.*,2005). The renewed interest in medicinal plants allowed researchers to investigate the antibacterial potential of some spices of medicinal background dating back to thousands of years, such as cinnamon bark. It was published that the essential oils of *Cinnamomum cassia* (bark) showed remarkable inhibitory effect against thee MDR-pathogens, namely, *E. coli, Pseudomonas aeruginosa,* and *S. aureus.* Moreover, it was observed that there is a considerable synergistic inhibition of that essential oil with *streptomycin* (El Atki *etal.,*2019).

The essential oils and cinnamaldehyde extracted from *Cinnamomum zeylanicum* showed good antibacterial activities against seven Gram-negative and nine Gram-positive fish pathogenic bacteria and recommended as a safe alternative to control bacterial infections in aquaculture(Pathirana *et al.,*2019). The main aim of this project was the characterization of natural products for *C. zeylanicum* and *C. longa* as antibacterial agents and their synergistic effect with Fucidic acid antibiotic.

MATERIALS AND METHODS

Plant Sample Collection

The plant materials used in this study consisted of *C. zeylanicum* and *C. longa* which are find in Iraq. These plants collected from different area in local markets/Baghdad city in November of 2021 [Table 1]. After that it was cleaned and isolated from foreign materials, crushed by an electric mill and then the powder was collected in plastic polythene bags and kept in the laboratory at room temperature until use.

Microbial Pathogens used for Antimicrobial Activities

The pathogenic microorganisms were used as a reference strains for testing the antimicrobial activities are listed in Table 2. Bacterial species selected for the study were one Gram-positive *S. aureus* and one Gram-negative *E. coli.* All the cultures of pathogenic strains were maintained on Brain Heart Infusion (BHI) agar medium (HiMedia) at 4°C for further experiments. The cells were inoculated and incubated at 37°C in Mueller-Hilton broth for 12 h before the screening procedure.

Culture Media

Types of media were required for carrying out this study, Brain Heart Infusion broth, MacConkey agar, Nutrient agar, and Mannitol Salt Agarand Mueller-Hinton agar (MHA) (HiMedia), according to (Atlas *et al*., 2004; Jawtez, *et al*., 2010).

Antibiotic

Antibiotic used includes: Fucidic acid, Table 3 shows antibiotic potency.

Preparation of Aquatic Extracts for Antimicrobial Activity

C. zeylanicum and *C. longa* were collected from Local markets/Baghdad city. Dried plants were

Table 1: Plant materials used in this study

Plant	Part used	Place	Time of collection
Cinnamomum zeylanicum	Bark	Local markets/ Baghdad city	November
Curcuma longa	Rhizomatous	Local markets/ Baghdad city	November

Table 2: Microorganisms used in this study

Strains	Source
Staphylococcus aureus	Al-Nahrain university, college of Biotechnology
Escherichiacoli	Al-Nahrain university, college of Biotechnology

Table 3: List of antibiotic

Antibiotic	Antibiotics concentration	Company/Origin
Fucidic acid	30 μg	Samarra/Iraq

grinded and prepared for extraction. For aqueous extraction, a quantity of 1 g of dried powder (*C. zeylanicum* and *C. longa*) was mixed with 25 mL distilled water. The mixture was left in oven at 45°C for 24 h [Figure 1] and preparation of plant extracts standard concentrations. 1 g of each aqueous extract (dry) was taken and the aqueous extract was dissolved in 100 mL sterile distilled water. Then, filtered by filter paper Wattman, No. 1, the supernatant was collected at an interval of 2 h, we have a stock solution and concentration to 100 and 200 mg/mL and then used as antimicrobial activity (Almola, 2010).

Antimicrobial Activity by Well Diffusion Method Assay

The antimicrobial activity of *C. zeylanicum* and *C. longa* extracts was tested using the agar well diffusion method against bacteria *S. aureus* and *E. coli*. According to Obeidat *et al*. 2012, an inoculum suspension was swabbed uniformly to solidified 20 mL MHA for bacteria and the inoculum was allowed to dry for 5 min. Holes of 6 mm in diameter were made in the seeded agar using glass pasteur pipettes. Aliquot of 20 µL from each plant crude extract (100 and 200 mg/mL) was added into each well on the seeded medium and allowed to stand on the bench for 1 h for proper diffusion and thereafter incubated at 37°C for 24 h. The resulting inhibition zones were measured in millimeters (mm).

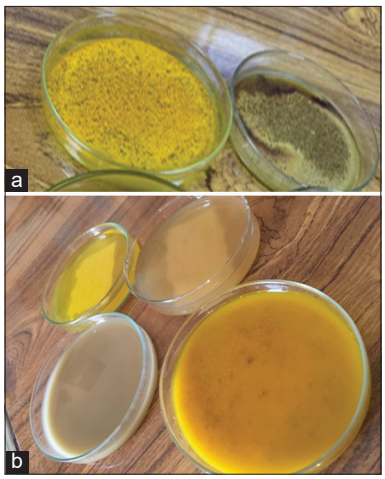

Figure 1: (a and b) *Cinnamomum zeylanicum* and *Curcuma longa*

Synergistic Effect of Plant Extract with Antibiotics against Bacteria Pathogens

The bacterial cultures were grown in Mueller-Hinton broth at 37°C. After 4 h of growth, each bacteria was inoculated on the surface of MHA plates. Subsequently, the antibiotic and Fucidic acid (50 mg) were placed on the surface of each inoculated plate and then added 20 µL of plant extract (at a concentration of 200 mg/mL, to identify synergies effect between the plant extract and antibiotics, while to identify synergies between the plant extract and antibiotics, 20 µL of antibiotics and 20 µL of plant extracts were mixed and put together on a filter paper disk which was left for 1 h to dry. The plates were incubated at 37°C for 24 h. The diameters of clearing zones were measured.

RESULTS AND DISCUSSION

Evaluation of Plant Extracts Bioactivity

Against E. coli

The results in Table 4 revealed that the well diffusion method evaluated the antimicrobial activity of plant extracts against *E. coli*. *C. longa* was showed the highest effect against *E. coli* with a zone of inhibition 13 and 14.5 mm at a concentration of 100 and 200 mg/mL, respectively. Antimicrobial activity was observed by *C. zeylanicum*, with a zone of inhibition 9 and 13.9 mm. at a concentration of 100 and 200 mg/mL, respectively, as shown in Table 4.

Against *S. aureus*

The results in Table 5 revealed that the well diffusion method evaluated the antimicrobial activity of plant extracts against *S. aureus*. *C. longa* was showed the highest effect against *S. aureus* with a zone of inhibition 11 and 16.8 mm at a concentration of 100 and 200 mg/mL, respectively. No antimicrobial activity was observed by *C. zeylanicum*, at a concentration of 100 mg/mL and a zone of inhibition 10 mm at a concentration of 200 mg/mL as shown in Table 5.

However, among the estimated 250,000–400,000 plant species, only 6% have been studied for biological activity, and about 15% have been

investigated phytochemically. This shows a need for phytopharmacological evaluation of herbal drugs (Goyal *et al.,* 2007). The medicinal value of plants lies in some chemical substances that produce a definite physiological action on the human body. These phytochemicals are the active constituents that exhibit some biological activities concerning antioxidant, antimicrobial, anti-inflammatory, and anticancer activities (Goyal *et al.,* 2007). The most important phytochemicals are alkaloids, flavanoids, tannins, and some other phenolic compounds which are abundantly found in plants (*Duraipandiyan et al.,* 2006).

Plants as a source of medicinal compounds have continued to play a dominant role in the maintenance of human health since ancient times. According to the World Health Organization, plant extracts or their active constituents are used as folk medicine in traditional therapies of 80% of the world's population. Over 50% of all modern clinical drugs are of natural product origin (Kirbag *et al.,* 2009).

Antimicrobial agents are the important chemicals that are widely used in modern medical practice thanks to their disease treatment features by eliminating or killing the infecting microorganisms. There are a various number of antimicrobial agents currently available. When selecting for a particular antimicrobial agent, its selective toxicity must be evaluated. Because the antimicrobial agent is desired to exhibit greater toxicity to the infecting pathogens then to the host organism (Atlas *et al*., 2004).

Table 4: Antimicrobial activity of *Cinnamomum zeylanicum* and *Curcuma longa* extracts by well diffusion method against *Escherichia coli*

Concentration of extracts (mg/mL)	Inhibition zone (mm) by *Cinnamomum zeylanicum* extracts	Inhibition zone (mm) by *Curcuma longa* extracts
100	9	13
200	13.9	14.5

Table 5: Antimicrobial Activity of *Cinnamomum zeylanicum* and *Curcuma longa* extracts by well diffusion method against *Staphylococcus aureus*

Concentration of extracts (mg/mL)	Inhibition zone (mm) by *Cinnamomum zeylanicum* extracts	Inhibition zone (mm) by *Curcuma longa* extracts
100	No inhibition zone	11
200	10	16.8

Mohamed *et al.* 2010, evaluated the chemical constituents and biological activities of Artemisia herba-alba. Only the essential oil was found to be active against some Gram-positive bacteria (*Streptococcus hemolyticus* and *S. aureus*) and Gram-negative bacteria (*E. coli, Shigella sonnei,* and *Salmonella typhosa*).

Abubakar (2010). Studied evaluated plants as antibacterial use crude leaf extracts of Eucalyptus camaldulensis against some pathogenic bacteria, was least activity in terms 25 of zones of growth inhibition was shown by aqueous extract against *E. coli* (7 mm), *K. pneumoniae* (9 mm), *Proteus mirabilis* (13 mm), *S. typhi* (12 mm), and *S. aureus* (12 mm) while the highest was demonstrated by the acetone, with a recorded zone diameter for *E. coli* (12 mm), *K. pneumoniae* (13 mm), *Salmonella typhyi* (14 mm), *P. mirabilis* (15 mm), and *S. aureus* (14 mm) (Abubakar, 2010). Development of bacterial resistance to the available antibiotics and increasing popularity of traditional medicine has led researchers to investigate the antibacterial compounds in plants. *C. longa* is a medicinal plant that botanically is related to Zingiberaceae family (Chattopadhyay *et al.,* 2004). *C. longa*, commonly known as "turmeric," is widely used as a spice and coloring agent and is well known for its medicinal properties (Luthra *et al.,* 2001). Components of turmeric are named curcuminoids, which include mainly curcumin (diferuloyl methane), demethoxycurcumin, and bisdemethoxycurcumin (Chainani-Wu, 2003). Curcumin is the most important fraction which is responsible for the biological activities of turmeric. The melting point of curcumin, $C_2H_2OO_6$, is 184°C. It is soluble in ethanol and acetone, but insoluble in water (Joe *et al.,* 2004). Curcumin 95%, a potent antioxidant, is believed to be the most bioactive and soothing portion of the herb turmeric and possess the properties like antioxidant, anti-inflammatory, anti-platelet, and cholesterol lowering antibacterial and anti-fungal effects. It contains a mixture of powerful antioxidant phytonutrients known as curcuminoids and inhibits cancer at initiation, promotion, and progression stages of tumor development. It is a strong anti-oxidant, which supports colon health, exerts neuroprotective activity, and helps to

maintain a healthy cardiovascular system (Luthra *et al.,* 2001).

C. longa oil was tested against cultures of *Staphylococcus albus, S. aureus,* and *Bacillus typhosus*, inhibiting the growth of *S. albus and S. aureus* in concentrations up to 1–5000 (Chopra *et al.,* 1941). Many *C. longa* species are traditionally used for their medicinal properties. Antifungal, antibacterial, and antiflamatory activity has been reported for species such as *C. longa, C. zedoaria, C. aromatic, and C. amada* (Yoshioka *et al.,* 1998; Negi *et al.,* 1999; Majumdar *et al.,* 2000). It is evident from the results that *B. subtilis* was the most sensitive organism to *C. longa* extract of curcuminoid and oil. Wilson *et al.,* (2005) reported that antibacterial activity of ethanol extract of *C. zedoaria* (0.15 mg/mL) and *C. malabarica* (0.94 mg/mL) showed higher inhibition against *B. subtilis* and their ethanol extracts were effective only at higher concentration of 3.75 mg/well. Both the species of turmeric gave MIC against *B. subtilis* was 8.0 mm in diameter. It has been reported that Gram-positive bacteria are more sensitive to plant oil and extract (Karaman *et al.,* 2003).

Alzoreky and Nakahara, (2003) studied that among Gram-positive bacteria, *B. cereus* was the most sensitive organism to *C. longa* extract and its ethanol extract gave MIC 12.0 mm in diameter. Eloff (2001) reported antibacterial activities against *S. aureus*, *Pseudomonas aeruginosa*, *E. coli,* and *Enterococcus faecalis* using acetone extracts of bark and leaves of *Sclerocarya birrea* with MIC values from 0.15 to 3 mg/mL.

Evaluation of Fucidic Acid Antibiotic Activity against Bacteria Pathogens

The results in Table 6 revealed that the well diffusion method evaluated the antibioticsactivity of Fucidic acid (50 mg and 100 mg) against *S. aureus* and *E. coli*. Fucidic acid was showed effectiveness against *S. aureus* and *E. coli* with a zone of inhibition 15 and 17 mm at a concentration of 50 mg, respectively. While it was zone of inhibition 17.4 and 19 mm at a concentration of 100 mg against *S. aureus* and *E. coli,* respectively [Table 6].

In the study showed that acidic pH has been shown to improve the activity of fusidic acid against *S. aureus* (Biedenbach *et al.,* 2010). This may be of particular importance for treatment of staphylococcal infections developing in acidic compartments (Weinrick *et al.,* 2004), such as the skin, vagina, and urinary tract, and for eradication of intracellular forms of *S. aureus*, which are also exposed to an acidic pH.

In the study, McGhee *et al.,* 2011 tested the MICs of fusidic acid (CEM-102) plus other agents against 40 methicillin-resistant *S. aureus* (MRSA) isolates from cystic fibrosis patients and the activities of fusidic acid with or without tobramycin or amikacin against *Pseudomonas aeruginosa*, MRSA, and *Burkholderia cepacia* isolates from cystic fibrosis patients in a 24-h time-kill study. Fusidic acid was potent (MICs, 0.125–0.5 μg/mL; a single 500-mg dose of fusidic acid at 8 h averaged 8–12. 5 μg/mL with 91–97% protein binding) against all MRSA strains. No antagonism was observed; synergy occurred for one MRSA strain treated with fusidic acid plus tobramycin.

Synergistic Effect of Plant Extracts with Fucidic acid Antibiotic against Bacteria Pathogens

Aqueous extract increase the impact of antibiotics on the bacteria when it is added on them. However, it has led to increase the impact of antibiotics on the bacteria when it is added on them. The bacterial cultures were grown in Mueller-Hinton broth at 37°C. After 4 h of growth, each bacteria was inoculated on the surface of MHA plates.

Subsequently, the antibiotic Fucidic acid (50 mg) was placed on the surface of each inoculated plate and then added 20 μL of plant extract at a concentration of 200 mg/mL, to identify synergies

Table 6: Evaluation of Fucidic acid activity against *Staphylococcus aureus* and *Escherichia coli* by well diffusion method

Concentration of Fucidic acid (mg)	Inhibition zone (mm) of *Staphylococcus aureus*	Inhibition zone (mm) of *Escherichia coli*
50	15	17
100	17.4	19

effect between the plant extract and antibiotics. The synergistic effect between plant extract and antibiotics, we evaluated *in vitro* synergism between extracts of *C. zeylanicum* and *C. longa* extracts and antimicrobial drugs utilized against *S. aureus* and *E. coli* using well diffusion method.[1-10]

Against *E. coli*

C. zeylanicum and *C. longa* extracts and antibiotics are shown in Table 7 and Figure 2. C. *zeylanicum* extract has the best synergistic effect on *E. coli* when added with Fucidic acid. Extract of *C. zeylanicum* increased the effectiveness of Fucidic acid against *E.coli* (17 mm). As for the *C. longa* extract was the results with Fucidic acid on the bacteria (22 mm).[11-25]

Against *S. aureus*

C. zeylanicum and *C. longa* extracts and antibiotic as shown in Table 8 and Figure 2. *C. zeylanicum* extract has the best synergistic effect on *S. aureus* when added with Fucidic acid. Extract of *C. zeylanicum* increased the effectiveness each of Fucidic acid against *S. aureus* (18.6 mm). As for the *C. longa* extract was the results (when added to antibiotic) almost similar to *C. zeylanicum* extract, where it also has increased the impact of Fucidic acid on the bacteria (20.4 mm).

In our study, the plant extracts had different synergistic ability to inhibit the growth of microorganism depending on the method of extraction. Plants antimicrobials have been found to be synergistic enhancers in that though they may not have any antimicrobial properties alone, but when they are taken concurrently with standard drugs they enhance the effect of that drug (Rakholiya and Chanda, 2012).[26-50]

Drug synergism between known antibiotics and bioactive plant extracts is a novel concept and could be beneficial (synergistic or additive interaction) or deleterious (antagonistic or toxic outcome) (Adwan and Mhanna, 2008). Despite the abundant literature about the antimicrobial properties of plant extracts, none of the plant derived chemicals have successfully been used for clinical use as antibiotics (Adwan and Mhanna, 2008).

In recent years, the Infectious Diseases Society of America has highlighted a group of pathogens ESKAPE that they currently cause the majority of hospital infections and can effectively "escape" the biocidal action of antibiotics. *S. aureus* and *K. pneumoniae* are members in this group which includes Enterococcus faecium, *S. aureus*, *K. pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa*, and *Enterobacter* species (Boucher *et al*., 2009). The steadily increasing in multidrug-resistant bacteria to existing antibiotics is a serious problem that significantly causing treatment failure of infections and increase mortality rates (Harbarth and Samore 2005). There is an urgent need to develop new

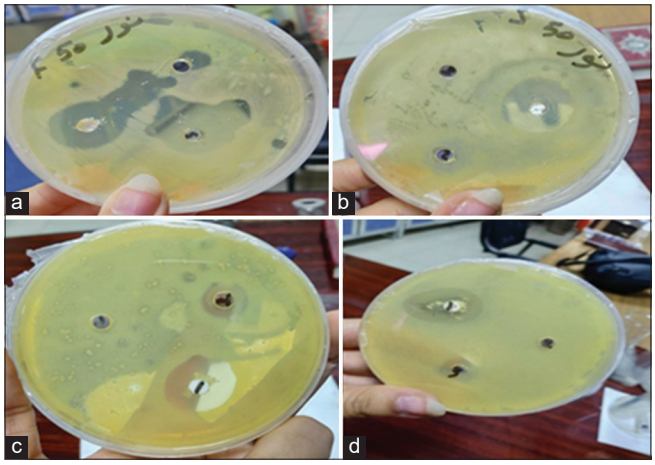

Figure 2: (a-d) Synergism between antibiotics and *Cinnamomum zeylanicum* and *Curcuma longa* extracts against bacteria pathogens

Table 7: Synergism between antibiotics and *Cinnamomum zeylanicum* and *Curcuma longa* extracts against *Escherichia coli*

Synergism between antibiotic and plant extracts	Inhibition zone (mm) of *Escherichia coli*
Cinnamomum zeylanicum extract with Fucidic acid	17
Curcuma longa extract with Fucidic acid	22

Table 8: Synergism between antibiotics and *Cinnamomum zeylanicum* and *Curcuma longa* extracts against *Staphylococcus aureus*

Synergism between antibiotics and plant extracts	Inhibition zone (mm) of *Staphylococcus aureus*
Cinnamomum zeylanicum extract with Fucidic acid	18.6
Curcuma longa extract with Fucidic acid	20.4

antibacterial substances or new compounds that block resistance mechanisms and improve treatment to eradicate these resistant strains. Treatment with antibacterial combinations, using two or more antibacterial agents, is one of the most important strategies to overcome multidrug-resistant organism (Torella *et al.,* 2010).

Recently, plant antimicrobials have been found to be synergistic enhancers in that though they may not have any antimicrobial properties alone, but when they are taken concurrently with standard drugs they enhance the effect of that drug (Darwish and Aburjai, 2010).

There are some generally accepted mechanisms of this interaction, including inhibition of protective enzymes, combination of membrane active agents, sequential inhibition of common biochemical pathways, and the use of membranotropic agents to enhance the diffusion of other antimicrobials (Bassolé and Juliani, 2012).

Phytotherapy has many potentially significant advantages associated with the synergistic interactions such as increased efficiency, reduction of undesirable effects, increase in the stability or bioavailability of the free agents, and obtaining an adequate therapeutic effect with relatively small doses, when compared with a synthetic medication (Aiyegoro and Okoh, 2009).

During the past 10 years, several reviews substantiated the effectiveness of combinations of plants with conventional antimicrobials (Aiyegoro and Okoh, 2009). However, no studies were found that investigated the effect of combination of *Thymbra spicata* extract with antibiotics against multidrug (MDR) *S. aureus* and *K. pneumoniae*. *T. spicata*, (Lamiaceae), is a native plant in the flora of Syria (Mouterde, 1983). It is an evergreen perennial shrub that tends to grow to 0.5 m on dry and sunny hillsides and high dry meadows (Barakata *et al*., 2013).

It is a well-known medicinal plant that used in folk medicine traditions. The essential oil found in different parts of *T. spicata* makes it an important antibacterial and antioxidant natural source. The infusion of this plant is used for treating of respiratory and sore throat infection. Besides, it used as a spice that gives a good flavor and taste to meals (Marković *et al*., 2011).

It is well known that antimicrobial activities of plant extract against tested bacteria differed, depending on location (Celiktas *et al*., 2007). Hence, the aim of the present study was to examine antibacterial effect of different *T. spicata* extract against multidrug-resistant strains of *S. aureus* and *K. pneumoniae* and to investigate the synergy between these extracts and commonly used antibiotics.

The study of hexane and ethanol turmeric react and curcuminoids (from ethyl acetate extract of curcuminoids isolated from *C. longa* with 86.5% curcumin value) against 24 pathogenic bacteria isolated from the chicken and shrimp showed the highest antimicrobial for ethanol extract with the MIC value of 3.91–125 ppt (Lawhavinit *et al*., 2010). The hexane and methanol extracts of *C. longa* demonstrated antibacterial effect against 13 bacteria, namely, *Vibrio harveyi, V. alginolyticus, V. vulnificus, V. parahaemolyticus, V. cholerae, Bacillus subtilis, B. cereus, Aeromonas hydrophila, Streptococcus agalactiae, S. aureus, S. intermedius, S. epidermidis,* and *Edward siellatarda.* However, curcuminoids elicited inhibitory activities against eight bacteria of *S. agalactiae, S. intermedius, S. epidermidis, S. aureus, A. hydrophila, B. subtilis,* and *B. cereus*. Hexane extract and curcuminoids exhibited the MIC values of 125–1000 ppt and 3.91–500 ppt, respectively (Lawhavinit *et al*., 2010). Indeed, it was shown that the addition of 0.3% (w/v) of aqueous curcumin extract to the cheese caused the reduction in bacterial counts of *Salmonella typhimurium, Pseudomonas aeruginosa*, and *E. coli* 0157:H7.

Moreover, it has decreased the *S. aureus, B. cereus,* and *Listeria* monocytogenes contamination after 14 days of cold storage period (Hosny *et al.,* 2011). Turmeric oil as a byproduct from curcumin manufacture also was found effective against *B. subtilis, B. coagulans, B. cereus, Staph. aureus, E. coli,* and *P. aeruginosa* (Negi *et al*., 1999). Curcumin also exhibited inhibitory activity on methicillin-resistant *S. aureus* strains (MRSA) with MIC value of 125–250 ug/mL (Mun *et al*., 2013).

The *in vitro* investigation of three new compounds of curcumin, namely, indium curcumin, indium diacetyl curcumin, and diacetyl curcumin, against *S. aureus*, *S. epidermis*, E. coli, and *P. aeruginosa* revealed that indium curcumin had a better antibacterial effect compared to curcumin itself and it may be a good compound for further *in vivo* studies. However,

diacetylcurcumin did not exhibit any antibacterial effect against tested bacteria (Tajbakhsh *et al.,* 2008). These results demonstrated promising antibacterial activity for different curcumin derivatives as well. The stability and assembly of FtsZ protofilaments as a crucial factor for bacterial cytokinesis are introduced as a possible drug target for antibacterial agents. Curcumin suppressed the *B. subtilis* cytokinesis through induction of filamentation. It also without significantly affecting the segregation and organization of the nucleoids markedly suppressed the cytokinetic Z-Ring formation in *B. subtilis* (Rai *et al*., 2008).

It was demonstrated that curcumin reduces the bundling of FtsZ protofilaments associated with the binding ability to FtsZ with a dissociation constant of 7.3 μM. It showed that curcumin through inhibition of assembly dynamics of FtsZ in the Z-Ring can possibly suppress the bacterial cell proliferation as one of the probable antibacterial mechanisms of action (Rai *et al*., 2008).[51-56]

The essential oil of *Cinnamomum verum* bark tested against four food-borne bacterial pathogens (Gram-positives and Gram-negatives), it exhibited strong antibacterial activity against all tested bacteria and recommended as a natural preservative in the food industry (Vazirian *et al.,* 2015). Another study was also evaluated the antibacterial potential of crude bark extract of little-investigated Indonesian cinnamon (*C. burmannii*) against five food-borne bacteria (*S. aureus, Bacillus cereus, L. monocytogenes, Salmonella anatum,* and *E. coli*) and recorded efficient antibacterial activity (Shan *et al*., 2007). A study on barks of four cinnamon species (*C. cassia, C. loureiroi, C. burmannii, and C. wilsonii*), all investigated plants showed varied remarkable antibacterial activity against food-borne pathogens (*S. aureus, L. monocytogenes, E. coli O157:H7, and Salmonella anatum*) (Liang *et.al*.,2019). The ethanol extract bark of Cinnamomum burmannii was examined against nine bacterial strains isolated from patients attending a dental clinic suffering from dental caries, results revealed that the extract is significantly inhibited all *Streptococcus spp*., and accordingly recommended as mouthwash (Waty *et al*., 2018). The essential oil of *Cinnamomum aromaticum* was effective against four enteropathogenic bacterial isolates associated with neonatal calve's diarrhea (*Klebsiella* spp., *Kluyvera* spp., *E. coli* F17*,* and *E. coli* F5) and recorded remarkable minimum inhibitory concentration as low as 0.625 μL/mL (Ammar *et.al*., 2017). *C. zeylanicum* exhibited significant activity against some extended-spectrum beta-lactamase-producing bacterial strains, namely, Escherichia coli and *Pseudomonas aeruginosa* (Hamedo. 2015).

CONCLUSION

According to the results antibacterial effect of *Cinnamomum zeylanicu*m and *Curcuma longa* extracts and their synergistic effect with antibiotic Fucidic acid against *Escherichia coli* and *Staphylococcus aureus*.

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